INFORMED CONSENT FORM -A

GENERAL INFORMATION OF A BIOAVAILABILITY/BIOEQUIVALENCE STUDY IN HEALTHY, ADULT, HUMAN SUBJECTS CONDUCTED AT CLINICAL PHARMACOLOGY UNIT, RANBAXY LABS LTD.

Dear Volunteer,

This document has been prepared to provide information required for your participation in a bioavailability/bioequivalence study. Please read this information and clarify if you have any queries before you decide to participate in the study.

- This is a research based study. You are being asked to participate in this research study.
- Take all the time you need to read and understand the information, before agreeing to participate in this study.
- If you are not able to understand any part of this document, please feel free to get your doubts clarified. An oral presentation of this document will also be held in the language you understand.
- Please sign the informed consent forms (A and B) and submit it for our records. You will be provided a copy of the same for your reference and record.
- During your participation in the clinical study, you will act as an independent individual, and not as an agent, partner or an employee of Ranbaxy Laboratories Limited.

PURPOSE OF THE STUDY

Bioavailability is the amount of a drug that becomes available in the body (eg: blood, urine) after consuming the drug. Two drugs are said be bioequivalent if the amount of drug in the body (eg: blood, urine) are similar after consuming the drugs.

Bioequivalence has to be proven between the marketed drug named reference and the generic drug (to be marketed) named test. Government agencies check the details of the results from the bioequivalence studies. When they are convinced that the two drugs are similar (bioequivalent), the test drug may be approved for marketing

Signature of Volunteer
GENERAL PROCEDURE OF A BIOAVAILABILITY/BIOEQUIVALENCE STUDY

Given below is a general explanation of how a bioavailability/bioequivalence study is conducted.

You will be admitted to the study if you pass the screening tests and provide a written informed consent. On day of admission, breath test for alcohol, drug of abuse in urine and or other tests if required by the protocol will be done in each period. Baggage and pocket(s) will be checked prior to admission and you are not allowed to carry alcohol, xanthine, tobacco, cigarette, illicit drug, medicine in any form, any eatables (solid and liquid) and any electrical or battery operated appliances other than wrist watch and mobile phone without camera. You will be provided with Ranbaxy volunteer uniform(s) during your in-house stay. During your participation in this study, you will be provided lockers to keep your belongings and an identity card which will be required to be displayed during in-house stay. You may be monitored (e.g. through Close Circuit TV-camera) during your stay at CPU.

During the stay in the unit you will be provided standardised meal. (For detailed meal plan refer to study summary in INFORMED CONSENT FORM - B).

You will be required to consume one of the study drugs (either the test or reference) in each period.

As per protocol, blood samples will be collected at pre-determined time intervals in vacutainers (tubes) through a disposable needle and cannula which will be inserted into a blood vessel and kept fixed at the site. To prevent the needle from getting blocked, solution of heparin (which is a normal body constituent) will be added. Half milliliter of heparinised blood will be discarded before sample collection. Alternatively, blood samples may also be collected, directly with a sterile disposable needle and syringe. The collected samples will be processed and stored appropriately for further analysis. (Please refer to INFORMED CONSENT FORM - B for Sample collection time points.)

As per the study requirement other biological specimen (e.g.: Urine, Stool, Sputum samples etc) may be collected at predetermined time intervals.

Pain, swelling and/or numbness of the arm may occasionally result from the blood collections during the study. This procedure may also occasionally cause light headness or fainting. These reactions are usually of short duration and are reversible.

After the completion of in-house stay, you will be discharged, with information to return on a specific date at a specific time for the subsequent period(s) of the study or for walk-in samples (ambulatory samples or for end of study safety sample), vitals signs measurement and adverse event monitoring, if required.

Signature of Volunteer_________________________
Similar procedures will be followed in the subsequent period(s) except for the informed consent procedure.

RESTRICTIONS TO BE FOLLOWED

If you participate in this study as a subject, you will be required to follow certain restrictions:

You will not be allowed to have tea, coffee, chocolates and cola during your stay in the unit. For 48 hours prior to admission and during the course of the study till last sample collection for pharmacokinetic analysis, you must not consume any alcohol or any products that contain alcohol (beverages, marinades, medicines, etc), grapefruit juice and/or grapefruit supplements. You must not have taken any medication including over the counter (OTC) medications 30 days before and throughout the study. Drinking water will be restricted before and after consuming the drug. Posture restriction will also be enforced after dosing. (For specific details of restrictions related to drinking water and posture, refer ICF - B).

BENEFITS

Since you do not require treatment with the study drug(s), you will receive no medical benefit from this study, other than the benefit of a free health check-up and the satisfaction of serving the interests of human beings in poor health.

NEW FINDINGS

Any new and important information which may be discovered during the study which may influence your willingness to continue in the study will be made available to you as soon as possible.

ALTERNATIVE TREATMENT

Since this study is for research only and the alternative would be not to participate.

INSURANCE POLICY

You are insured under the insurance policy no. OG-10-1113-3306-00000004 of Bajaj Allianz and you will be compensated in case of a trial related injury.

MAINTENANCE OF DISCIPLINE

You are expected to follow certain rules of the CPU and maintain discipline during your stay in the unit. In case you do not behave properly in the CPU you will be withdrawn from the study without any payment and/or excluded from participating in all future studies.

Signature of Volunteer
DETERMINATION OF FINANCIAL COMPENSATION DUE IN CASES NOT COMPLETING THE STUDY

1. Withdrawn from the study by the Investigator on objective medical grounds to safeguard your health, before administration of study drug
   - On pro-rata basis

2. Withdrawn from the study by the Investigator on objective medical grounds to safeguard your health, after administration of study drug
   - Full payment on completion of study/ follow-up visits

3. Dropped-out of the study, on your own accord, after administration of study drug
   - On pro-rata basis

4. Dropped from the study on compassionate grounds, with the permission of Investigator
   - On pro-rata basis

5. Withdrawn from the study by the Investigator due to your failure to comply with the requirements of the study
   - On pro-rata basis

6. Withdrawn from the study by the Investigator because of your wilful withholding of information regarding your past or present medical illness(es) relevant to the study and your misbehaviour during the study
   - No payment

7. Non-compliance with the prescribed time-schedule for the follow-up visit (where applicable)
   - 50% of the payment due for that visit

CONFIDENTIALITY

Records of your participation in this study will be confidential so far as permitted by law. However, the confidential data which identifies you by name will be available to the study personnel, Corporate Quality Assurance Auditor during audits and to the Institutional Review Board (IRB) & various regulatory agencies, as it becomes necessary. Any publication of the data will not identify you by name. Investigator’s representatives/designates shall act as data custodian for this study till it is sent for archiving.

MEDICAL TREATMENT FOR INJURY

In case of study related side effect(s), medical care will be offered at the Clinical Pharmacology Unit and treatment of side effect or event requiring hospitalization will be carried out at a nearby hospital and the expenses will be borne by Ranbaxy Laboratories Limited

VOLUNTARY NATURE OF PARTICIPATION

Your participation in this study is entirely your choice. Whether you choose to participate or not will not involve any penalty or affect your selection for any future studies. You

Signature of Volunteer __________________________
may also stop participating in the research at any time you wish. It is your choice and all your rights will be respected.

**Note:** The Investigator can stop your participation in the study if the following are known— it appears to be harmful to your health; you fail to fulfill study requirements; you have withheld information related to your health record; the study is cancelled.

In case of emergency you can also call the study personnel by pressing the emergency bell which is available in the ward and toilet areas.

**CONTACT DETAILS**

At any time before, during or after the study, you can obtain further information about this study. In case of medical emergencies during the study, or if you have any urgent questions or queries concerning discomfort or injury associated with the study, please contact, Investigator at Ranbaxy Clinical Pharmacology Unit, Majeedia Hospital 2nd Floor, Hamdard Nagar, New Delhi 110 062, Telephone: 2995-6721.

If you have questions regarding your rights as a research subject, you may call Dr. Farhan Jalees Ahmad, Convener/Member Secretary, Jamia Hamdard Institutional Review Board (Telephone number 9810720387).

**Note:** You may also consult your family doctor at any time during the study

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Signature of Volunteer
INFORMED CONSENT FORM- B (STUDY INFORMATION)

Comparative bioavailability study of single oral-dose of two batches of olopatadine hydrochloride 10 mg extended release tablet of Ranbaxy Laboratories Limited with two oral doses of ALLELOCK® 5 mg tablets in healthy, adult, human male subjects under fed condition

Version No. : 01
Date : 16 July 2010
Supersedes : Not Applicable

This document provides information regarding this bioavailability study. Please read this information and clarify if you have any queries before you decide to participate in this study. If you agree to participate, please sign the document and submit for our records.

This study involves research to evaluate the amount of drug in the blood after administration of an extended release tablet formulation containing olopatadine hydrochloride 10 mg or two doses of ALLELOCK® 5 mg tablets (each dose containing olopatadine hydrochloride 5 mg administered 12 hourly; total dose 10 mg) in each period of the study.

Olopatadine is a selective histamine H1-receptor antagonist possessing inhibitory effects on the release of inflammatory lipid mediators such as leukotriene and thromboxane from human polymorphonuclear leukocytes and eosinophils. It is indicated for allergic rhinitis, urticaria, itching, resulting from skin diseases (eczema/dermatitis, prurigo, pruritus cutaneous, psoriasis, vulgaris and multiform exudative erythema).

In this three period study, single oral dose of two batches of olopatadine hydrochloride 10 mg extended release tablets of Ranbaxy Laboratories Limited, India will be compared with two doses of reference product, ALLELOCK® 5 mg tablets (each dose containing olopatadine hydrochloride 5 mg administered 12 hourly; total dose 10 mg) of Kyowa Hakko Kogyo Co. Ltd., Japan, when administered in 15 healthy, adult, human male subjects under fed condition.

ADVERSE EVENTS

The commonly reported adverse reactions are hepatic function disorder with increases in level of SGOT, SGPT, γ-GGT, LDH and ALP, etc., jaundice and sleepiness. Other adverse reactions reported during the clinical trials which occurred at an incidence of < 5% ≥ 0.1% are:

- Rash including erythema (redness of skin), edema (face, extremities, etc)
- Malaise (lack of health), dizziness, headache/ dull headache, thirst.
- Abdominal discomfort, abdominal pain, diarrhea, nausea
- Leukocytosis, leucopenia, eosinophilia, lymphopenia

Note: You can participate in this study if you have hemoglobin ≥ 13.0 g/dL.

Signature of Volunteer ___________________________
You cannot participate in this study if you have:

- History of hypersensitivity to olopatadine or any other related drugs.
- History of chronic headache.
- History of abdominal discomfort, diarrhea and/or nausea in the preceding week.
- History of hepatic function disorder and/or jaundice.
- History of any sleep disorder.
- Have a history of drug induced pruritis and/or rash.

Note:
- If you feel unwell or experience any uneasiness, please bring to the notice of the Medical Officer/Nurse/staff on duty immediately.

CAUTION: Avoid operating machines or driving vehicles during the conduct of the study.

FINANCIAL COMPENSATION

The compensation in this study will be Rs.7,250/- (Rupees Seven thousand two hundred and fifty only) per subject completing the study. From this, a sum of Rs. 500/- will be given to you after satisfactory resolution of the end of the study safety assessment(s). This is to compensate you for discomfort and inconvenience.

If you refuse to have your baggage searched at admission or you are uncooperative during the conduct of the study procedures you will be discharged without any payment.

STUDY SUMMARY

<table>
<thead>
<tr>
<th>Sampling schedule</th>
<th>Test (A or B): Pre-dose (in duplicate) and at 0.250, 0.500, 0.750, 1.000, 1.500, 2.000, 2.500, 3.000, 3.500, 4.000, 5.000, 6.000, 7.000, 8.000, 10.000, 12.000, 16.000, 24.000, 30.000 and 36.000 hours post dose in the respective periods.</th>
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<tr>
<td></td>
<td>Reference (R): Pre-dose (in duplicate) and 0.167, 0.250, 0.333, 0.500, 0.667, 0.833, 1.000, 1.333, 1.667, 2.000, 2.500, 3.000, 4.000, 6.000, 8.000,10.000, 12.000, 12.167, 12.250, 12.333, 12.500, 12.667, 12.833, 13.000, 13.333, 13.667, 14.000, 14.500, 15.000, 16.000, 18.000, 20.000, 24.000, 30.000 and 36.000 hours after administration of morning dose in the respective period.</td>
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<td>Blood Volume</td>
<td>A total 78 draws, 4-mL/sample (excluding duplicate pre-dose samples), 12 mL for predose duplicate sample, 16 mL for screening, 34.5 mL discarded blood and 08 ml for safety analysis at the end of the study; 382.5 mL total blood volume per subject. For Test (A or B): The volume of blood collected from predose blood sample</td>
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Signature of Volunteer__________________________
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<th><strong>Ambulatory Visit</strong></th>
<th><strong>Meal schedule</strong></th>
<th><strong>Washout period</strong></th>
<th><strong>Housing</strong></th>
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<td>None</td>
<td>After an overnight fast of at least 10 hours, you will be served high-fat high-calorie breakfast and it is required to be consumed within 45 minutes. Morning dose will be provided 45 minutes after the start of high fat high calorie breakfast in each period. Evening dose (of reference product) will be administered after 45 minutes of high-fat high-calorie dinner. You will receive lunch, snacks, dinner, breakfast, lunch and snacks at 4, 9, 11.25, 24, 28 and 33 hours post-morning dose, respectively.</td>
<td>At least 05 days</td>
<td>At least 11 hours prior to dose until 36 hours post-dose.</td>
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<th><strong>Restrictions</strong></th>
<th><strong>Clinical Safety Measurements</strong></th>
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<tr>
<td>You will be required to fast overnight for at least 10 hours before starting the breakfast. Dose will be administered with 240 mL of drinking water at an ambient temperature, 45 minutes after starting of high-fat high-calorie breakfast in each period. Evening dose (reference product) will be administered after 45 minutes of high-fat high-calorie dinner. Drinking water will not be allowed from 1 hour before dosing until 2 hours post-dose except 240 ml of drinking water given during administration of the dose (for evening dose of reference product also). After receiving the study drug, you will be required to sit upright or remain ambulatory for 2 hours, thereafter you can resume only normal activities while avoiding vigorous exercise. However, should medical events occur at any time during housing you will be placed in an appropriate position or will be permitted to lie down on your right side.</td>
<td>Adverse event monitoring and vital signs – oral temperature, sitting BP and radial pulse will be done after admission, prior to morning dosing and at 2, 10, 14, 22 and 36 hours post-morning dose in the each period. Vital signs shall be recorded within ±2.0 hours in each period. Brief clinical examination of the subject will be done at admission and at discharge in each period. The laboratory parameters like Hemoglobin, Total WBC count, Platelets, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils, Total Bilirubin, serum creatinine, blood urea nitrogen, serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), serum alkaline phosphatase, blood glucose (fasting/random) and serum cholesterol will be repeated at the end of the study, in case you have been administered the study drug. In case any of the above-mentioned laboratory parameter(s) is (are) outside the acceptable limits for laboratory parameters, you will have to come for follow up until the results are normal / clinically not significant.</td>
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Signature of Volunteer
| **Treatments** | Reference (R): ALLELOCK® 5 mg tablet of Kyowa Hakko Kogyo Co. Ltd., Japan.  
Test (A or B): Olopatadine hydrochloride 10 mg extended release tablet of Ranbaxy Laboratories Limited, India. |
| **Dose** | A single oral dose of Olopatadine hydrochloride 10 mg extended release tablet (Test: A or B) will be administered 45 minutes after the start of high-fat high-calorie breakfast.  
Two oral doses of ALLELOCK® 5 mg tablets (each dose containing olopatadine hydrochloride 5 mg administered 12 hourly; total dose 10 mg) in each period of the study. Morning dose will be administered 45 minutes after the start of high-fatt high-calorie breakfast. Evening dose will be administered 45 minutes after the start of high-fat high-calorie dinner during each period of the study. Dosing will be done under supervision of trained study personnel. |

Signature of Volunteer ______________________
DECLARATION

I hereby declare that:
- My participation in this study is voluntary.
- This study is a research project and provides me no medical benefits.
- I have the right to be provided with answers to questions arising during the course of the study.
- I will be provided any significant new findings coming to light during the research investigation.
- I can withdraw from the study at any time without prejudice to future medical care or selection for future studies.
- I can be withdrawn from the study at any time if I violate the study protocols or to protect my health.
- I have read and understood the Informed consent form and have no problem(s) in complying with the study protocol.
- My reference number with respect to volunteer enrolment of Ranbaxy Laboratories Ltd. is RLL_MAJ
- I currently require no medical treatment or care.
- I have withheld no information regarding my past medical history and current drug intake.
- I have read the consent form and any questions I had about the study, possible side effects or the consent form, have been answered to my satisfaction.
- I voluntarily give my consent for my personal data related to any information relating to me, as I have provided in the enrollment form, or as it is generated during screening and study procedures, including identification number, or factors specific to my physical, physiological, mental, economic, cultural or social identity, to be processed as required for the study requirements. I also voluntarily give my consent for the processing of data.
- I am aware that my biological samples shall be anonymized or destroyed as per the requirements of the procedures of the study.
- It is my right to obtain information at reasonable intervals and without excessive delay regarding whether or not data relating to me are being processed.
- It is my right that, unless required by law, or while fulfilling a contract, with suitable measures to safeguard my legitimate interests: “No automated processing of my personal data shall be done which makes me subject to a automated decision, produces legal effects concerning me or significantly affects me.”
- “No automated processing of my personal data shall be done to evaluate certain personal aspects relating to me, such as my performance at work, creditworthiness, reliability, conduct, etc.”
- During the past 90 days I have not participated in any experimental studies conducted here or elsewhere.
- I will maintain discipline during my stay at the Jamia Hamdard campus.
- If I have any further questions regarding this research study or in the event of research related injury, I may contact Investigator (011-2995-6721) or Dr. Tauqif Monir, Study Director (91-124-4231001). I may contact Dr. Farhan Jalees Ahmad, Convener/Member Secretary, Jamia Hamdard Institutional Review Board (Telephone number 9810720387), if I have any questions regarding my rights as a volunteer.
- My signature confirms that consent is based on information provided and that I had freely chosen to participate without prejudice.

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<tr>
<th>Volunteer's Signature &amp; Date/ Thumb impression*</th>
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<tr>
<td>Impartial witness’s Signature &amp; Date*</td>
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<tr>
<td>Impartial witness’s Name and his/her relation with Volunteer</td>
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<tr>
<td>I here by declare that I have no relation with Ranbaxy</td>
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<tr>
<td>Signature of Person Obtaining Consent &amp; Date</td>
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<tr>
<td>Investigator’s Signature &amp; Date</td>
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* In case of illiterate volunteer

Declaration: I have received the signed copy of this ICF (Form A & Form B)
Volunteer’s Signature & Date: ...........................................